TARGETED HIV AND STI SCREENING STRATEGIES AMONGST MSM IN BALTIMORE, AND THE IMPACT ON THE HIV EPIDEMIC: Using Agent Based Models to Study STI- HIV Co-infection Dynamics

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by
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Abstract:

Co-infection of men who have sex with men who have sex with men (MSM) with HIV and and *Neisseria gonorrhoeae/Chlamydia trachomatis* (NG/CT) remains a significant public health problem in the United States due to co-infection dynamics creating an epidemiologic phenomenon whereby co-epidemics of HIV and NG/CT (along with other STIs) help propagate each other**.** One of the key components of the US National AIDS Strategy revolves around the HIV Care Continuum, in which HIV infected persons are diagnosed, linked to care, retained in care and virally suppressed to prevent transmission. Screening for HIV is the entry point for the care continuum and various understanding the most efficacious strategies for this is of utmost importance to help identify HIV infected persons and link them to care. We used an agent-based model to test three screening strategies for efficacy: targeting high risk MSM, increased general HIV screening, and improved NG/CT screening amongst HIV infected MSM.

Targeting high risk MSM and increased general HIV screening produced significant decreases in the HIV and NG/CT incidence relative to baseline; but the former produced steeper declines while simultaneously testing thousands less persons. Improved NG/CT screening amongst HIV infected MSM has no impact on the incidence rate of either. The targeting high-risk MSM strategy produced steep declines in HIV incidence, and efficiently achieved this in less HIV tests given per year compared to the general HIV screening. This suggests that targeting high risk MSM may be a more effective approach to achieve reduction in HIV incidence. Furthermore it suggests that the HIV epidemic amongst MSM in Baltimore may be concentrated amongst a subset of the MSM population.

Preface

This work was borne out of a longstanding interest in HIV infection in the MSM population. This manuscript and project would not have been realized without the help of a several key people. I would like to thank Dr. Parastu Kasaie and Dr. David Dowdy for giving me the opportunity to pursue this thesis question in the first place, and their unwavering support, mentorship, and advice over the past year. I would also like to thank Dr. Kenrad Nelson and Dr. David Holtgrave for their advice and mentorship during my time at JHSPH, and for always make time availed for me. Fran Burman has been an invaluable resource over the past two years and completing this thesis and my master's degree would not have been possible without her. My fellow classmates have also been an incredible source of encouragement as well, and I thank them for always being there for me. I would also like to thank Jeffrey Freeman, Pranay Randad, and Ian Sanchez, for dealing with my nerves and quirks, giving me advice when I needed to hear it but didn't necessarily want it, and being steadfast in their support of me. Lastly I would like to thank my parents, Ethan and Julie, and my brothers, Noah and Nate, for their unconditional love and never-ending encouragement.

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Introduction

Co-infection of men who have sex with men who have sex with men (MSM) with HIV and and *Neisseria gonorrhoeae/Chlamydia trachomatis* (NG/CT) remains a significant public health problem as this results in increased transmissibility of these diseases. HIV infection is a particularly large problem in Baltimore City, which has one of the highest rates of HIV in the US at 7 times the national average.[57] HIV transmission is further modified by co-epidemics of other sexually transmitted infections (STIs.)[33] HIV/STI co-infected individuals are more likely to transmit the disease, and STI infected individuals are more likely to acquire HIV.[33] HIV, chlamydia, and gonorrhea, infections particularly impact men who have sex with men (MSM). Per the Centers for Disease Control (CDC) guidelines, sexually active MSM should be screened *for Neisseria gonorrhoeae/Chlamydia trachomatis* (NG/CT) at least every year, and every 3-6 months if at higher risk (e.g. infected with HIV).[58] Yet in Baltimore, this annual screening rarely reaches 40%.[24] Once a person is diagnosed with NG/CT, they given a one-time treatment of antibiotics to cure and clear the infection.

Gonorrhea infection has been shown to be associated with an increased risk for HIV aquisistion.[59] Several studies have suggested that coinfection with HIV, gonorrhea and syphilis increase viral load, and subsequently viral shedding, resulting in increased risk of HIV transmission by co-infected individuals.[60] Furthermore, gonorrhea and chlamydia infection can enhance the risk of HIV acquisition via inflammation, disruption of the genital mucosa and increased numbers of active immune cells.[61] While gonorrhea

and chlamydia are non-ulcerative STIs (whereas ulcerative STIs increase the risk of HIV transmission and acquisition more substantively), it has been posited that the far greater prevalence of these two STIs in the general population makes them potent modifiers of HIV transmission dynamics, particularly amongst MSM.[61] Gonorrhea and chlamydia infection have been found to statistically significantly increase the odds of HIV acquisition by 1.8, creating an epidemiologic phenomenon whereby co-epidemics of HIV and NG/CT (along with other STIs) help propagate each other.[62] This in turn suggests that measures to combat one of these diseases may in turn decrease the incidence of the other.

Furthermore, some of the key HIV prevention strategies involves encouraging safe sex practices (e.g. condom use), behavioral change, pre-exposure prophylaxis (PrEP) and treatment as prevention (TasP) via highly active antiretroviral therapy (ART). [63–66] Getting persons engaged in HIV care and treatment is critical for both preventing progression to AIDS amongst HIV-positive individuals and preventing the spread of HIV within a population via the TasP strategy. Once a person is diagnosed with HIV infection, the goal is link the patient to care providers, prescribe the patient antiretrovirals (ART), have the patient adhere to ART, and retain them in care. This pathway from diagnosis, to treatment, to retention, to maintained viral suppression is referred to as the HIV Care Continuum.[67,68] As such, increasing knowledge of HIV status, linking and retaining those infected in care, and improving drug adherence is critical to controlling the disease in populations. Particularly, screening for HIV and subsequent diagnosis is important since it is the entry point to the care continuum. However, there is some debate as to the best way to increasing screening and outreach in the MSM.[69] Often, the approach is to use

general HIV "know your status" screening events, which aim to increase general uptake of HIV screening in communities. Given that certain sub populations of MSM can be prone to higher risk and higher transmission of HIV, targeting these populations for increased screening may prove more effective. Conversely, given co-infection dynamics of NG/CT and HIV that suggest they may help increase transmission of the other; improved NG/CT screening amongst HIV infected MSM may also be an effective targeted screening strategy to link persons to the care continuum.

HIV Natural History and Epidemiology in the United States

HIV is the second largest cause of death by an infectious disease in the world. In the United States, HIV is not a major cause of mortality, but a significant cause of morbidity. HIV is most commonly transmitted via sexual intercourse; however, transmission can also occur vertically from mother to child, via blood transfusion, and through contaminated needles.[70] Several key populations are at higher risk for HIV acquisition due to social and biological factors, chiefly sexual behavior.[71] When a person is initially infected with HIV the virus enters the acute phase. HIV infects cells presenting the molecule CD4 on the surface, using CD4 along with other cell surface molecules to enter the cell and replicate. Initially the immune system is able to control the infection, leading to a reduction in viral load and a slight increase of CD4 T cells.[71] However HIV then enters a stage where it infects CD4 cells at lower levels that do not trigger an extensive immune response.[71] As HIV kills more CD4 T cells, the body's ability to mount an adaptive response to the virus is diminished and viral load begins the climb. If CD4 count falls below 200 cells/ml, the person develops AIDS, and has great difficulty

mounting an immune response against any invading pathogen.[71] In the absence of treatment, this can lead to death from an opportunistic infection and a range of other debilitating symptoms.

In the US, HIV is quite prevalent but not a significant cause of mortality any longer.[67] Current US HIV/AIDS policy is driven mostly around the HIV Care Continuum and preventing new infections. The 2015 update to the United States National HIV-AIDS Strategy has ambitious goals, including: increasing serostatus awareness among those living with HIV to 90%, reducing the number of new diagnoses by 25%, increasing to 85% the number of persons linked to HIV care within one month of their diagnosis, increasing the percentage of persons retained in HIV care to 90%, and increasing the percentage of persons diagnosed with HIV who are virally suppressed to 80%.[67]. Per NHAS, the goal is "The United States will become a place where new HIV infections are rare, and when they do occur, every person, regardless of age, gender, race/ethnicity, sexual orientation, gender identity, or socio-economic circumstance, will have unfettered access to high quality, life-extending care, free from stigma and discrimination."[67] The HIV care continuum is an integral part of this strategy, and the collaboration across the federal government is critical to improve each step of the HIV Care Continuum.[24] While the care continuum is just part of the overall plan (with other areas focused on behavioral, social, and educational interventions to prevent new HIV infections), it is a key component to assist persons already living with HIV and to reduce their chances of transmitting the infection to others.[67,68] The report also notes that STI clinics are where many people get tested and receive their HIV diagnosis; 1 in 10 MSM receive their HIV diagnosis within one year of being diagnosed with rectal gonorrhea and syphilis.[67]

Understanding how the STI clinic plays a role in linking MSM to HIV Care and the overall Care Continuum will help illustrate how the clinic plays a role in, and reduces barriers to, this linkage to HIV care.

Barriers to the HIV Care Continuum include late HIV diagnosis, suboptimal linkage to care, poor retention in HIV care, poor ARV adherence, viral resistance to ARV medications, and insufficient use of ARVs.[72] Understanding and reducing the impact of these barriers is paramount to increasing the percentage of persons knowing their serostatus, engaged in care, and achieving viral suppression. Recent data suggests that in serdiscordant couples, ARV-achieved viral suppression has reduced the risk of HIV transmission from 92-98%, illustrating the importance of archiving viral suppression in HIV-infected individuals.[68] However, improving engagement in just one area of the care continuum doesn't have a major impact at the other levels; therefore, improvement across multiple, if not all levels is paramount to strengthening the care continuum.[68,72]

In the US, it is estimated that 1.2 million people are living with HIV, and of these, 13% do not know they were infected.[67] As previously noted, Baltimore has some of the highest rates of HIV and STI's in the United States.[57] In 2010 (the most recent publicly available data) the rate of new HIV diagnoses in Baltimore (77.6 per 100,000) was 7 times the national rate (16.3 per 100,000), and 3 times the Maryland rate (30.0 per 100,000). [57] In Maryland, the vast majority of HIV cases are concentrated in Baltimore, and HIV/AIDS is still a top 5 cause of death for adults in the city. [57] In 2012, the among men infected with primary and secondary syphilis , 60.1% were also co-infected with HIV. [57] HIV transmission in Baltimore is also highly concentrated amongst African-American MSM. [57]

Chlamydia and Gonorrhea Natural History and Epidemiology in the United States.

Chlamydia trachomatis and Neisseria gonorrhea are the most common bacterial sexually transmitted infections in the US. The majority of infections are asymptomatic, highlighting the importance of screening programs in reducing population chlamydia burden.[73] Transmission for both occurs during vaginal, anal, and oral sex and contact with infected tissues. Once a person is infected, chlamydia can establish a long term infection, with 50% of infected persons clearing the infection within one year, 80% within 2 years, and 90% within 3 years.[74] The immune response for Chlamydia typically involves neutrophil and monocyte mucosal infiltration and inflammation, which can result in long-term tissue damage and scarring in the event of persistent infection.[75,76] Chlamydia has several different clinical manifestations unique to men. These include urethritis, epididymitis, prostatitis, and proctitis, the latter of which is particularly common amongst MSM who have unprotected anal intercourse (UAI)**.**[73] In the absence of treatment proctitis can result in fever, anorectal pain and discharge, bleeding, and constipation. These symptoms also increase the potential for transmission, though are not required.[73,75]

Gonorrhea pathogenesis proceeds in 4 stages, attachment to the mucosal surface, local penetration and invasion, local proliferation, and lastly local inflammatory response or system distribution.[77] *Neisseria gonorrhoeae* has high levels of antigenic variation, which can make it difficult for the immune system to mount a specific response.[77,78] Antibiotic resistant *Neisseria gonorrhoeae* has also been reported, further complicating treatment and control. Urethritis is the most common symptom, though many cases are

asymptomatic.[78] Persons who are asymptomatic can transmit the bacterium to an uninfected partner.[79] On average about 50% of persons exposed to an infected male partner become infected, with that percentage rising to 93% with repeated exposures.[80]Gonorrhea and chlamydia often co-infect individuals in many populations.[73,75]

There exist several NG/CT tests, with the gold standard being nucleic acid amplification tests (NAATs), e.g. polymerase chain reactions (PCR).[73,75] Other tests include serology, antigen detection, and bacterial culture.[6] Screening for chlamydia is critical for disease control because of the high proportion of asymptomatic cases, the potential for long term infection, and the potential for re-infection with the causative organism.[75] Most public health programs regarding chlamydia prevention involve interrupting transmission by encouraging safe sex practices, and diagnosing and treating chlamydia cases can help achieve this goal.[75]

Chlamydia is the most commonly reported notifiable disease in the United States, with 1,526,658 cases reported in 2015, and rates increasing in recent years.[81] The overall prevalence of chlamydia in the population aged 14-39 years old was 1.7%.[81] Among MSM in the United states, the prevalence of chlamydia was 16%, and about 17% in Baltimore, illustrating the importance of targeting screening and prevention strategies this population. [10]

Furthermore, in the US in 2015, there were 395,216 cases of gonorrhea, with an overall rate in men of 140 cases per 100,000 persons [82] Amongst MSM, this rate was 1,474.4 cases per 100,000 MSM in 2013.[83] This difference in rates amongst men overall compared to the much higher rate amongst MSM alone, illustrates the disproportionate

burden of gonorrheal disease in MSM. In Baltimore, the prevalence of gonorrhea amongst MSM was 16.9%, which was in fact the lowest prevalence of gonorrheal disease amongst STI surveillance network sites. [82] Even with its relatively low prevalence, almost 1 in 5 MSM in Baltimore are infected with gonorrhea, illustrating a high burden of disease in this subpopulation. Given the complex epidemiological and biological interactions between gonorrhea, chlamydia, and HIV and the high burden in the MSM population in Baltimore, better understanding of the transmission dynamics and opportunities for control measures to be implemented is of the utmost importance.

Social and Epidemiological factors impacting HIV and STI transmission in MSM populations

Social factors impacting MSM transmission include high number of sexual partners, seroadaptive behaviors, ethnicity, and stigma. MSM can have higher number of sexual partners; thus magnifying their risk of acquiring HIV though multiple potentially infectious contacts. [38] This risk can be compounded by a behavior known as "bare backing" which is defined as deliberate avoidance of condom use.[84] This can lead to someone being infected more easily, and then spreading infection to others, which can speed the spread of HIV though a sexual network. [84] Furthermore, HIV is more common amongst ethnic minorities. In the US, black MSM are much more likely to become infected with HIV, not know their serostatus, and not be linked to healthcare because of economic and social factors limiting healthcare access. In turn, black MSM, compared to other MSM can be more likely to be living in poverty, be less educated, and more likely to be incarcerated.[84] Indeed, this in turn leads to black MSM also having less access to STI/HIV prevention education and items that could reduce the chance of infection, eg.

condoms.[84] Furthermore, MSM overall can be a stigmatized minority, which can make health care access and outreach challenging, and require extra effort in order to reach that community. MSM in certain regions of the United States, and the world, may be afraid to come forward and seek medical attention for fear of this identifying them as MSM.[38,84] Combatting these socio-structural barriers to health access is important to also help combat HIV.

Baltimore City HIV and STI Prevention

The Baltimore City Health Department (BCHD) operates 2 public STI clinics that offer STI/HIV counseling and care. These facilities offer both rapid (results delivered less than 30 mins) and conventional testing. If one tests positive, the person is offered confirmatory testing, partner services and linkage to primary care. In 2010, amongst persons attending these STI clinics, 89% of HIV positive persons them received at least post-test counseling. [57] BCHD also encourages local emergency departments (EDs) to screen for HIV and other STIs. [57] BCHD also screens via community based health organizations, such as Chase-Brexton Healthcare, which is the largest provider of health services to the MSM community in Baltimore. [57] BCHD has used syphilis epidemiological data to help direct where they should concentrate their HIV testing efforts. [57] Some locations beyond EDs and STI clinic's BHCD tests at are methadone clinics, LGBT events and homeless shelters, all provide providing to further link identify HIV infected persons and link them to care. [57] The Maryland Department of Hygiene and Mental Health (DHMH) issued a series of regulations aimed increasing the detection of HIV, via a new opt-out policy (as opposed to opt-in) whereby healthcare practitioners in

a range of settings offer diagnostic HIV testing and HIV screening as a part of routine clinical care for individuals ages 13-64. [57]

Once a person is diagnosed with HIV, they are offered post-test counseling and are linked to care. Care-Linkage Investigators (CLIs) will make phone-calls and field-visits to HIV infected persons to help them find care and partner-services. [57] Often, many efforts are made to locate clients after they test positive, but sometimes they are lost to follow up. This linkage to care initiative is part of the BCHDs Early Intervention Initiative. [57] To incentivize clients to show up for their second appointment, they are offered gift cards. The linkage to care strategy is as follows; 1) BCHD searches existing STI/HIV databases if the person has previously tested to understand their needs and potential services. [57] 2) Each person is prioritized in terms of the following a) knowledge of their HIV status, b) prior access to HIV partner counseling and referral services, and c) documentation of previous access to primary care. [57] 3) New clients are assigned a counselor who notifies them of their test results, offers them partner services and outlines their care options and where to receive care (eg. primary, and Ryan White funded services). [57] 4) Previously identified clients are assigned CLIs who help link the person to primary care. [57] 5) The persons are added to the STI-MIS database for documentation and data collection. [57]

Modeling STI and HIV Screening Strategies and Their Effects on the Epidemic

Agent based modeling is a method that attempts to simulate the interactions and actions of autonomous agents within a group to determine how these individual actions translate to macro-level effects. These models have several levels including individual agents who have certain actions/behavior patterns (e.g. an MSM who is in a monogamous

relationship), decision making and learning process for these agents, interaction rules, and an overall environment. Randomness is introduced to the model via Monte Carlo methods. The value of agent-based models is that they attempt to infer and predict complex behaviors and their macro-level effects from the collective effect of individual simple decision-making.

Screening for HIV and NG/CT are critical components to their control strategies. However, simply having general HIV or NG/CT screening might not be the most impactful approach to identify cases of these diseases; and linking those infected to care. Given the epidemiologic interaction between HIV transmission and NG/CT co-infection, and that being screened for NG/CT likely increases treatment uptake, simply meeting the CDC screening guidelines could have a significant impact on both the NG/CT and HIV epidemics in Baltimore city. This could lead to higher detection and treatment of NG/CT cases; and subsequently decrease the incidence of these diseases. Furthermore, MSM who are at high-risk for HIV and NG/CT infection due to age and sexual activity could be major drivers of the epidemic since they can potentially spread the infection to more people. Targeted screening in this population and linking infected persons to care could also have a significant impact on the HIV and NG/CT epidemics in Baltimore city. Conversely, increased screening for HIV and linking infected persons to care could not only decrease HIV incidence, but also potentially decrease NG/CT incidence This study will explore 3 screening scenarios and their impacts on HIV and NG/CT incidence in the MSM population in Baltimore over a 50-year period after their rollout. The scenarios explored are: 1) targeted screening of high-risk (defined as young and sexually active) MSM for both HIV and NG/CT testing; 2) a general HIV only screening program for

persons who present for STI care; and 3) testing the impact of increasing the proportion of HIV infected MSM screened for NG/CT and ultimately of meeting the CDC NG/CT screening guidelines for this population.

Methods

Agent Based Model to study MSM, HIV, and STI Outbreaks

Demographic Module

In this model agents are single MSM who are characterized by age, race, and neighborhood. Each agent is evaluated at every time step, which in this model is one week. At each time step the following are evaluated: the per act probability of HIV transmission, HIV testing probabilities, linkage to care probabilities in terms of engagement and disengagement, and probability of ART provision/viral suppression achieved. Transmission of HIV (modeled as a per sexual act probability) is determined by serodiscordant partnership status, frequency of sex act, safety of sex act, HIV stage of infected partner, and ART/PrEP use (Table 1).

The demography module determines the baseline population structure and controls the model procedures for aging, birth and death. The population modeled was MSM in Baltimore aged 15 to 75. The population in the model is structured by Baltimore's Community Statistical Areas (CSAs). There are 55 CSA's in Baltimore. Agents' in the model are defined by their CSA and race (white Caucasian, or Black African American.) Agents' age according to a simulated clock and exit the model based off by the age specific mortality rate, upon reaching age 75 or via the increase in mortality due to HIV infection. The population is replenished by a birth process which is

modelled using Poisson methods calibrated to each CSA's mean population. New persons enter the population at age 15 and are calibrated to CSA. Baltimore's MSM population size was estimated to be about 15000, based off of the population of men in Baltimore above the age of 15, and previously published percentages of MSM in the city.[85] Racial makeup of each CSA was arranged in levels, from 1-5, with each level being the proportion of that CSA population that was African American.

CSA groupings were made to determine how agents might interact with other people from other regions of the city. CSA groupings were determined by sharing a border and only differing by income and racial makeup by 1 level. These groupings continued by CSA's of similar status until they came into contact with CSA's that differed by more than 1 level. This procedure was followed for all groupings, and eventually 16 groupings were made. These groupings determined how individuals could interact and spread throughout the model.

Partnership Module.

The second module of the model is the sexual partnerships model which delineates how agents can form sexual partnerships There are two types of partnerships in the model, "stable" and "casual". Stable partnerships last for several years, whereas casual partnerships last only for a single week. As previously discussed, CSA are placed into neighboring groups to determine an agent's search area. If they are seeking a new partnership, agents can search for new partners in their own CSA, in neighboring CSAs and non-neighboring CSAs, each with a different probability. These probabilities govern the mixing patterns and clustering of sexual partnerships within a CSA, and then this

applied across the whole population. Then once this geographic search domain has been made, agents can establish partnerships, which is determined by a probability governed by age and race mixing. Individuals search their entire search domain in its entirety, potential partnerships are checked for compatibility, and incompatible ones are dissolved. Incompatibility is assessed regarding sexual positioning (insertive preference or receptive preference). Age mixing and race mixing parameters were based off of the BESURE study (The Baltimore branch of the National HIV Behavioral Surveillance System). At the end of each simulation week, partnerships are updated, and those who have reached their pre-specified duration are terminated. For those agents whose partnerships dissolved, they begin to search for new partnerships based via the geographic search domain based on where they live. They will select partners based on race and age-depending mixing patterns and on sexual role. An agent can engage in multiple casual partnerships from week to week, or can only be involved in, at most, one stable and one casual partnership at a time. An individual's probability of seeking out a new partnership is a probability based on their age and is fixed by age group. High-risk behavior is modeled as a function of age and number of sexual partners. The individual's sexual role preference is fixed at birth. There are also two parameters that govern whether or not an induvial will engage in a stable or casual partnership.

HIV Epidemiology Module

HIV infection is modeled as 3 disease states, acute infection (CD4 count > 500 cells/ul), chronic infection (CD4 count 200-500 cells /ul) and late infection (CD4 count < 200 cells/ul). The disease state determines an individual's CD4 count, mean viral load

(which was a measure of infectiousness), and HIV mortality rate. The disease state progression assumes the absence of antiretroviral therapy (ART). If an individual is on ART, depending on stage they start treatment, they will either remain in the chronic state or dwell in the late infection stage for 1 year before reverting back to the chronic stage. CD4 count is not modeled directly, but the disease state is based off of viral load, as that is a direct measure of infectivity.

The HIV continuum of care is modeled in 5 stages: 1) unaware of infection; 2) aware of infection status, but not linked to care; 3) linked to care, but not engaged; 4) engaged in care and on ART; and 5) engaged in care, but not on ART. At each time step HIV-positive persons have a probability for being screened for HIV, and subsequently if diagnosed, have a fixed probability of being linked to care. Once these persons are engaged in care, they start ART. These same persons, after starting ART, will have viral load decrease for the first few months, and then full viral suppression after that period. ART also lowers the mortality rate at each disease stage. Persons who start ART at the late infection stage (CD4 < 200 cells/ul) will have a mortality rate adjusted for ART for one year, before moving back to the chronic state (CD4 200-500 cells/ul). Persons can stop being engaged care and adhering to ART, and if this occurs they cannot restart ART for 6 months. These persons will also no longer be virally suppressed and experience a decrease in CD4 count. At each time step, persons who had disengaged in care, will have a weekly probability of restarting care. Persons re-continuing ART can move between the disease stages.

At each time step, for serodiscordant partnerships, transmission to the negative partner is evaluated. This transmission probability is determined by the infectivity (viral

load) of the infected partner, the negative partner's immunity, and the global transmission coefficient. The negative partner's immunity is a measure of their PrEP adherence, which is a value ranging from 0 to 1 determined by absence to full adherence to PrEP. The global transmission coefficient is a measure of the baseline rate of HIV transmission per contact.

Sexual role preference is assigned at birth (insertive, receptive, or versatile). Two persons who are both insertive or both receptive are considered to be incompatible partners within the model. If both partners are versatile, the type of act (receptive or insertive) is 50% for each man. The proportions of each sexual preference was calibrated by BESURE study data and is as follows: 42% insertive-only, 26% receptive-only, and 32% versatile.

Gonorrhea and Chlamydia Epidemiology Module

Gonorrhea and Chlamydia (NG/CT) in this module are assumed to be spread through sexual contact (oral and rectal). The dynamics of infection are modeled as a susceptible, infected, susceptible (SIS) model because there does not seem to be any protective immunity; therefore, once a person is recovered, they can be re-infected. Persons who are infected and have symptoms have a fixed probability of seeking care at each time step, and once seeking care, have a probability of being tested for NG/CT. If the test is positive, they are treated. Other care seeking episodes for other reasons for care will not result in a test and treatment for NG/CT. Persons who are on treatment are assumed to be infectious during treatment and for the week after. This type of testing is referred to as symptomatic testing behavior. MSM can also be regularly screened for

NG/CT as well per the CDCs recommendation based on MSM HIV status. Model Calibration

The model used BCHD data on HIV and NG/CT cases in Baltimore in order to simulate the HIV outbreak in Baltimore city. Parameters (such as incubation, HIV and NG/CT interaction, infectiousness, screening etc) were gleaned from a literature review and are presented in table 1. From the BCHD dataset, the prevalence of HIV amongst MSM is 3329 people. In our simulated MSM population of 15,000, this corresponds to a prevalence of 22%.

The BCHD dataset for gonorrhea contains all males in Baltimore with gonorrhea infection that were reported to the BCHD. These cases were reported between 1/1/09 and 5/31/16. The cases were restricted from 2011 until 2015 because in 2011, STI clinics switched to using the NAAT to diagnose syphilis, which is in line with the CDC's guidelines. Unfortunately, sexual identity was not included for the men in this dataset, however, certain persons diagnosed with NG were selected for a (STD Surveillance Network) SSuN interview, and amongst this dataset, 26-30% of these men identified as MSM.

The adjustment for persons not seeking care was based off literature parameters. About 60% of symptomatic persons do not seek out care. To account for this, the number of cases was increased by 150% to estimate the true number of actual cases. Furthermore, to adjust for asymptomatic cases, which would determine care-seeking behavior, the proportion of symptomatic cases reported in the literature was used. These proportions were 74% symptomatic for urethral, 20% for rectal, and 10% for pharyngeal.

The BCHD data for the proportion of HIV-infected MSM screened for NG/CT is 40%. To meet the CDC guidelines, this parameter in the model is set at 100%. This will model the effects of screening that meets the CDC guidelines regarding annual screening for HIV-infected MSM.

Simulation Calibration

The BESURE 2014 study provided detailed MSM social and sexual network data that was used to calibrate the partner structure in the model. The data included details on the average number of partners in the last 12 months, the type of partners by age-group, and stability of the partnerships to calibrate the proportions in the simulated MSM population in the model. [86] The simulation was run 200 times, and from that, the average distribution was determined. The parameters for the model are presented in table 1.

Testing for Effects of High Proportions of NG/CT Screening

To understand the effects of increased NG/CT screening on both the dynamics of the NG/CT epidemic and the HIV epidemic we tested 3 screening strategies with various levels of screening for each one. These scenarios were generated by manipulating 3 parameters in the model, the weekly probability of presenting to STI care and screening for HIV and NG/CT for high-risk MSM, the weekly probability of screening for HIV infection only in the general MSM population, and the probability of compliance with the CDC recommendation among HIV-infected MSM for presenting to STI care every 12 months and testing for NG/CT infection. The first 2 parameters were manipulated by modulating the weekly probability of screening relative to baseline, such that we ended up with 3 scenarios, twice (2x) as likely, four times (4x), and 8 times (8x)) for each of the

parameters. For the probability of compliance with the CDC recommendation among HIV-infected MSM for presenting to STI care every 12 months and testing for NG/CT infection parameter, this was arranged a proportion from 0 to 1, with proportions 0.4, 0.6, 0.8 and 1 as each scenario. This resulted in 4 experimental scenarios plus 1 baseline scenario for each of the 3 manipulated parameters, resulting in a total of 12 scenarios. Simulated data regarding incidence of symptomatic and asymptomatic NG/CT, prevalence of NG/CT in the population, persons screened for NG/CT, prevalence of HIV, incidence of HIV, HIV mortality and persons screened for HIV were obtained. The data output by the simulation was analyzed to determine the differences between the screening scenarios, and the effects on the NG/CT and HIV outbreaks.

Statistical Analysis

Analysis of variance (ANOVA) tests were used to determine the significance of difference between each of the scenarios, and the base line incidence or screening proportion. Graphs illustrating the trends in HIV incidence, persons screened for HIV, NG/CT incidence, and persons screened for NG/CT were generated for each of the 3 scenario groups as appropriate. All statistical analysis was done in R software version 3.3.1.

Results:

Targeting High-Risk MSM for HIV and NG/CT Screening

Impact on HIV Epidemic

4 total scenarios modeling the different impacts of targeted HIV and NG/CT screening were generated. These scenarios were the baseline (current scenario in

Baltimore) and the following modulated probabilities: twice (2x) as likely to present for screening, four times (4x), and 8 times (8x). The baseline scenario had relatively stable patterns of HIV and NG/CT incidence; with an average incidence per year of 1440 cases per 100,000 persons and 17,393 cases per 100,000 persons for HIV and NG/CT respectively. Under baseline conditions the incidence rate fluctuates very little over time. Additionally, an average of 6,756 HIV tests, along with an average 3,686 NG/CT tests are given annually.

The impacts of each of these scenarios on HIV incidence are depicted in Fig 1a. HIV incidence in the total population decreases over time for all non-baseline scenarios, and the magnitude of this decrease increases accordingly by scenario screening probability. Fig 1b shows the number of HIV tests given each year. The differences in HIV incidence per 15,000 persons per year (the population of the model) at years 10, 20, 30 and 40 are all statistically significantly different from baseline.

Further one-way ANOVA tests were completed to determine if there were differences between each of the increased screening scenarios to each other. The baseline level of HIV incidence amongst MSM in Baltimore in the model was 1,447 cases per 100,000 persons at year 10. At this same time point, the incidence rate fell to 1407 cases per 100,000 persons under the 2x screening scenario, 1380 cases per 100,000 persons under the 4x screening scenario, and 1353 cases per 100,000 persons under the 8x screening scenario. At year 30, these differences were more pronounced, with the model forecasting an incidence rate of 1440 cases per 100,000 persons under baseline conditions; and the incidence rate falling to 1373 cases per 100,000 persons under the 2x scenario, to 1307 cases per 100,000 persons under the 4x scenario, and 1260 cases per

100,000 persons under the 8x scenario. These represent decreases in incidence of 4.65%, 9.23%, 12.5% over a 30-year period for the 2x, 4x, and 8x screening scenarios respectively.

All screening scenarios start realizing a significant decline ($p<0.001$) in HIV prevalence after 20 years of continuous intervention. The 2x screening scenario does not start to show significant decreases in prevalence until year 10, and takes longer for the steep drop in prevalence to occur relative to the other scenarios, as seen in Fig 2. The drops in prevalence can be seen for all screening scenarios starting after 30 years of continuous intervention. As expected, the trend of the overall decrease in prevalence is mirrored by the increase in screening probability under each scenario. None of the scenarios seem to exhibit a plateauing in the prevalence over the first 40 years after intervention. HIV incidence is decreased significantly from current baseline levels of screening under each of these 3 increased screening of high-risk MSM scenarios, and that increasing the likelihood of screening significantly decreases HIV incidence between the scenarios as well.

To achieve these reductions in HIV incidence and prevalence, more MSM had to be screened. At baseline roughly 6,756 tests for HIV were given each year. The average number of tests for HIV per year jumped to 10,116 under the 2x scenario, 13,437 under the 4x scenario, and 16,733 under the 8x scenario. As was expected, the increase number of HIV tests in each scenario corresponded with a larger decrease in HIV incidence and prevalence.

Impact on NG/CT Epidemic

Figures 3a and 3b depict the impact of increased screening of high-risk MSM on NG/CT combined incidence and total screening levels per year. A similar pattern to HIV incidence is seen here, with all increased screening scenarios showing decreased NG/CT incidence over time, but the extent of the drop in NG/CT incidence is much greater than for HIV. The magnitude of the decrease in incidence is mirrored by the increased modeled probability of screening. As seen in Fig 3a, doubling the probability of screening amongst high-risk MSM has a noticeable impact on NG/CT incidence over time; with even greater decreases in incidence over time seen as screening probability increases (as modeled by scenario). The differences between NG/CT incidence per 15,000 persons at Years 10, 20, 30 and 40 are all statistically significant from baseline ($p < 0.001$). Under the baseline conditions at year 10, the rate of NG/CT is 17,387 per 100,000 persons. In the increased screening scenarios at year 10, the incidence rate is 16,067 cases per 100,000 persons under the 2x scenario, 14,660 cases per 100,000 persons under the 4x scenario, and 13,426 cases per 100,000 persons under the 8x scenario. At year 30, the baseline incidence of NG/CT is 17,393 cases per 100,000 persons. This incidence rate falls to 15,007 cases per 100,000 persons under the 2x scenario, 13,000 cases per 100,000 persons under the 4x scenario, and 11,213 cases per 100,000 persons under the 8x scenario. These represent decreases in incidence of 13.72%, 25%, 35.53% over a 30-year period for the 2x, 4x, and 8x screen scenarios respectively. Each of the scenarios evaluating increased screening amongst high-risk MSM and the impact on NG/CT incidence show significantly reduced incidence relative to baseline levels. Furthermore, each of these decreases are significantly different from

each other. There is also a similar decline in NG/CT prevalence seen (Figure 4). As expected, the steepest declines in NG/CT prevalence are seen in the scenario with the highest screening probability. Unlike the trend seen in HIV prevalence, NG/CT prevalence seems to plateau in all scenarios after 40 years on continuous intervention. Regardless, significant declines are seen in all scenarios by year 20.

The number of tests for NG/CT under each scenario increased as expected. At baseline, the average number of tests for NG/CT per year was 3686. This number of tests given per year for NG/CT rose to an average of 7253 under the 2x scenario, 10,586 under the 4x scenario, and 14,266 under the 8x scenario. The increases in tests given corresponded to respective decreases in NG/CT incidence and prevalence.

A General Increased Screening Program for HIV

Impact on HIV Epidemic

This screening strategy modeled the effect of increased general HIV screening in the MSM community, akin to a sustained "know your status" testing effort. The strategy modeled the general impact of increased HIV screening on HIV and NG/CT incidence by exploring the impact of 4 scenarios, which were the baseline (current scenario in Baltimore) and the following modulated probabilities; twice (2x) as likely, four times (4x), and 8 times (8x). The impact of each of baseline and the 3 increased screening scenarios on HIV incidence and total number of people screened per year are presented in Figs 5a and 5b. Fig 5a depicts the impacts of each scenario relative to baseline (Scenario 11) on HIV incidence over time.

All increased screening scenarios illustrated reduced HIV incidence over time, with the magnitude of this decrease affected by each scenario's increased screening probability. The graph depicts most differences in HIV incidence amongst all scenarios relative to baseline can be seen after 30 years of continuous intervention; with the scenarios modeling higher screening probability depicting faster reductions in incidence. The differences between HIV incidence at years 10, 20, 30, and 40 are significantly reduced from baseline for just the 4x screening scenario and the 8x screening scenario, assuming a significance level of $p < 0.05$. The 2x screening scenario had a statistically significantly reduced incidence rate of HIV different from baseline when measured at years 30 and 40 ($p < 0.05$), but not when measured at years 10 and 20. The baseline incidence rate of HIV at year 10 was 1,433 cases per 100,000 persons. At year 10, the 2x screening scenario did not show any reduction in HIV incidence with 1433 cases per 100,000 persons. However, at the same time point, the 4x and 8x screening scenarios respectively showed statistically significant decreases in HIV incidence, with the 4x screening scenario showing a reduction to 1,413 cases per 100,000 persons, and the 8x screening scenario showing a reduction to 1407 cases per 10,000 persons. At year 30, the baseline rate of HIV is still 1433 cases per 100,000 persons. All screening scenarios at year 30 show statistically significant reductions in HIV incidence; with the 2x scenario showing a reduction to 1420 cases per 10,000 persons, the 4x scenario showing a reduction to 1387 cases per 100,000 persons, and the 8x scenario showing a reduction to 1360 cases per 100,000 persons. These represent decreases in HIV incidence of 0.9%, 3.2%, and 5.1% over a 30-year period for the 2x, 4x, and 8x screening scenarios respectively. To test for difference between each of the screening scenarios, one-way

ANOVA's were also run to determine differences in the mean incidence rate at year 10. The tests showed at that this time point, the HIV incidence rate is significantly different between all increased screening scenarios. Fig 5b depicts the impact of each scenario relative to baseline on total persons screened for HIV. Each scenario shows a similar pattern of an increase in tests given for HIV initially before leveling off. However, this yearly amount HIV tests givens varies noticeably between of the three scenarios, with the 8x scenario depicting the largest increase in HIV tests given relative to the other scenarios. In this set of scenarios, we also observe slight fluctuating trends in HIV prevalence, with no clear evidence of a decline in HIV prevalence within 30 years after starting the intervention (Fig 6).

To achieve these decreases in HIV incidence and prevalence, more HIV tests were administered. The average number of HIV tests given per year at baseline was 6,753 MSM. This increased to 9,368 HIV tests given per year under the 2x scenario, 14,596 under the 4x scenario, and 25051 under the 8x scenario. The increase in HIV tests given corresponded to larger declines in HIV incidence and prevalence in each scenario.

Impact on the NG/CT Epidemic

The impact of increased general HIV screening on NG/CT incidence is depicted in figure 7. Observed declines in incidence are only seen after 25 years of continuous intervention, and all scenarios here exhibit the pattern of NG/CT incidence stabilizing around year 40. There appears to be differences in NG/CT incidence by scenario. To determine if any of these observed differences were statistically significant, one-way ANOVA tests were performed between each scenario at years 25, 30, 40 and 50 and baseline. The 2x, 4x, and 8x, screening scenarios only showed a significantly ($p < 0.01$)

reduced incidence rate different from baseline measured at years 30 and 40. To test for differences between each scenario, one way- ANOVA tests were also conducted. These were compared at Years 10, 20, 30, and 40. These results illustrate that there is some fluctuation in NG/CT incidence between the increased screening scenarios; but after year 30 significant differences ($p<0.05$) in NG/CT incidence rates become more apparent, and the trend continues for the rest of the scenario. This is seen in figure 8. At year 30, the baseline rate of NG/CT is 17367 cases per 100,000 persons. All screening scenarios show significantly reduced incidence of NG/CT; with the 2x scenario showing a reduction to 17,007 cases cases per 100,000 persons, the 4x scenario showing a reduction to 16,613 cases per 10,000 persons, and the 8x scenario showing a reduction to 16,400 cases per cases per 10,000 persons. These represent decreases in NG/CT incidence over a 30-year period of 2.07%, 4.24%, and 5.56% respectively.

Interestingly the pattern of each scenario's impact on NG/CT prevalence almost exactly mirrors that of the pattern of NG/CT incidence (Fig 8). We again see NG/CT prevalence diverge slightly in the first few years before beginning to decline for good around year 20 for all scenarios. The magnitude in the decline again mirrors the increase in screening probability by scenario. The declines in prevalence are significant for all scenarios starting at year 30, but this decline plateaus in year 40, just 10 years later. This reflected in both the trend seen in fig 8, and in the close test statistical year 30 and 40 for each scenario.

Increased screening for NG/CT Amongst HIV-Infected MSM

Impact on the HIV Epidemic

To model the impact of increasing the proportion of HIV-infected MSM screened for NG/CT, a set of scenarios were run that modeled this proportion relative to baseline (0.4) The scenario proportions for 0.6, 0.8 and 1 (the CDC recommended screening guideline). Each of these scenarios assume that persons testing positive will be treated for NG/CT and rendered no longer infectious, also impacting the HIV/NG/CT co-infection parameter. Additionally, all scenarios assume that there is no increase in HIV testing beyond baseline. The impact of increasing the proportion of HIV infected MSM screened on HIV incidence is shown in Figure 9.

There does not appear to be any impact on HIV incidence by increasing the proportion of HIV infected MSM screened. The baseline (0.4) and the other 3 scenarios (screening proportions 0.6, 0.8, and 1) do not appear to result in any significant differences in incidence over time, as the incidence lines overlap throughout the whole 50-year model run period. ANOVA tests conducted to test differences in incidence rate at different time points confirmed this observation. Increasing the proportion of HIV of infected MSM from NG/CT also does not appear to impact HIV prevalence (Fig 10). The range of prevalence in the Baltimore MSM population ranges from from 3210 cases to 3250 cases, a range of only 40 cases. One-way ANOVA tests confirm the lack of difference in prevalence between scenario.

Impact on the NG/CT Epidemic

There does appear to be a difference in NG/CT incidence over time as seen in Fig 11a. These differences appear slight, relative to the other two scenario groups.

Furthermore, the differences in NG/CT incidence become observable at a later time point relative to the other screening strategies, with these differences becoming noticeable around year 40. Similar to the trend seen in NG/CT incidence, there appears to little impact on NG/CT prevalence as well (fig 12). One-way ANOVA tests confirm that significant declines in prevalence only start to be see at year 40 and level off ($p < 0.001$). Tests were conducted until year 50, to in order to capture the full trend of N/CT prevalence.

Comparing HIV Screening Strategies

While both the targeted screening and general HIV screening strategies resulted in decreases incidence in both diseases, the magnitude of the decrease and the number HIV tests given to achieve the decrease differed greatly between strategies (tables 2 and 3). The least aggressive screening scenario (the 2x scenario) for targeting high-risk MSM resulted in a roughly 5% decrease in HIV incidence, and achieved this by an average of 10,116 HIV tests given per year. The scenario in the general HIV screening strategy that most closely realizes these decreases in HIV incidence is the 8x screening scenario (a 5.1% reduction), which was achieved giving an average of 25,051 HIV tests per year. In order to achieve the same decrease in HIV incidence, the general HIV screening model had to give nearly 15,000 more HIV tests compared to the 2x increased screening in the high-risk MSM screening strategy, 148% more MSM relative to the 2x scenario. In other terms for the 2x targeted screening scenario, just giving 2,175 tests annually led to a 1% decrease in HIV incidence over a 30-year period, compared to under the 8x general screening scenario where 4,912 tests had to be given annually to achieve same result. Therefore, despite giving more HIV tests, the most intensive general screening strategy

barely outperformed the least aggressive high-risk MSM screening strategy. To further accentuate this disparity in HIV tests given versus reduction in HIV incidence, the 8x (most aggressive) screening strategy targeting high-risk MSM resulted in a 12.5% reduction in HIV incidence, and achieved this by giving 16,733 HIV tests per year. Thus despite giving 8,313 HIV tests less than the comparable general HIV screening strategy, the reduction in incidence was more than doubled. Of further note, the 8x targeted screening scenario achieved a 1% reduction in HIV incidence more efficiently than the 2x targeted screening scenario, with just 1,338 tests given annually compared with 2,175 tests given annually.

Discussion

Of the three screening strategies tested, targeting high-risk MSM, improving general HIV screening, and increasing the proportion of HIV-infected MSM screened for NG/CT; only the scenarios that increased targeted high-risk MSM and general HIV screening strategies showed consistent reductions in HIV or NG/CT incidence. The results here illustrate that targeting this specific MSM subpopulation can result in a profound reduction in the HIV and NG/CT epidemics in Baltimore while requiring substantially less HIV and NG/CT testing. While high-risk young MSM can be a more difficult population to reach for HIV testing[87,88], it may be a better use of HIV control resources and effort to target them for HIV and NGCT testing; as evidenced by the reductions in tests given to achieve a 1% reduction in HIV incidence in the MSM population as a whole. For HIV control programs faced with limited resources and

budgets, using less HIV tests to target high-risk MSM can produce far greater reductions in HIV incidence than a general screening program, allowing for gains in program efficiency while using less resources, assuming the trade-off for reaching this population is lower than the number of tests saved. Furthermore, the substantial reduction in incidence in the overall population being brought about by targeting a subset of the population suggests that the high-risk subpopulation, which is mostly comprised of young MSM (YMSM) has a higher burden of HIV relative to the general MSM population, with HIV transmission and infection being partially localized within this group. Conversely, there could be a higher number of persons in this population who are unaware of their HIV infection and due to a higher propensity of engaging in casual partnerships, are more likely to transmit the virus. Still, the difference in the impact on HIV incidence in each screening scenarios suggests retrospectively, at least in Baltimore, the HIV epidemic is concentrated in the YMSM high-risk population.

While the differences in NG/CT incidence decline were expected, as the general HIV screening strategy did not test for NG/CT and the screening strategy targeting high-risk MSM did, the difference in reduction of NG/CT was noticeable. The 8x screening scenario for the general HIV screening strategy resulted in a 5.56% decrease in NG/CT incidence after 30 years and achieved this by giving 25,051 NG/CT tests per year; whereas the 2x screening scenario targeting high-risk MSM resulted in a 13.72% reduction in NG/CT incidence after 30 years by just giving 10,586 NG/CT tests per year. While certainly directly testing for NG/CT and linking those persons to treatment under the high-risk MSM screening strategy explains the disparity in incidence decline, the difference in number of persons screened versus decline in incidence is striking in its

magnitude. That the 4x and 8x high-risk screening scenario achieved 25% and 35% reductions in NG/CT incidence by giving fewer NG/CT tests per year is notable given the high incidence rate of NG/CT in the general MSM population. This could be due to a higher burden of NG/CT in the high-risk subpopulation, but clearly targeting them for increased screening and treatment can result in a marked reduction in NG/CT incidence amongst the MSM population in Baltimore. While is this scenario there was not the perfect comparison to a general NG/CT screening strategy, the magnitude of the decrease in NG/CT suggests that, as noted with HIV above, the NG/CT epidemic amongst MSM in Baltimore is concentrated in this subpopulation of YMSM. Additionally, it is encouraging that the general HIV screening strategy did in fact reduce NG/CT incidence even though NG/CT was not directly targeted by this intervention, as it supports the idea that co-epidemics of NG/CT help propagate each other. Thus, improving screening of HIV and subsequently linking infected persons to care can have a radiating impact on other STI co-epidemics, resulting in incidence reduction of NG/CT, and possibly other STIs; and therefore could be considered as part of an integrated STI (HIV and others) control strategy. Further research could shed light on the impacts of other STI's, such as syphilis, and the impacts of improved screening and treatment on HIV and NG/CT epidemics.

Increasing the proportion of HIV-infected MSM screened for NG/CT had no impact on HIV incidence and prevalence, and little impact on NG/CT incidence and prevalence. This could be due to the fact that the HIV-Infected MSM population is already a small subset of the overall MSM population, and amongst that group, those also infected and who will become infected with NG/CT is an even smaller group. Therefore,

since this strategy is targeting only a small segment of the population, it had little impact on either epidemic Future research could focus on the impact of general NG/CT screening and its impact on the NG/CT and HIV incidence, and comparing that to the targeted screening strategy.

There is a dearth of agent-based HIV modelling studies, but the conclusions here agree with the existing body of literature on modelling HIV screening. Brookmeyer et al used an agent based model to study the percentage of cases of HIV prevented using a various components and combinations of HIV prevention strategies.[88] In the scenario evaluating general HIV testing alone, where testing was increased 150%, they found that this prevented 4.9% of HIV cases.[88] This is akin to the strategy in our model evaluating general increased HIV screening, whereby the most intensive scenario has a similar 5% reduction in HIV incidence. Similarly, a compartmental model developed by Sorensen et al found that doubling the annual testing rate (akin to the 2x screening scenario for general HIV screening) in New York City could potentially reduce the prevalence of HIV by 5% from projected levels over a 20 year period.[89] While this is a notable improvement over the reduction in prevalence in the 2x general (0.9% reduction) HIV screening scenario in our model, the different methodology in this modelling approach (in that agent-based models arguably better capture stochastic dynamics of epidemics than compartment based models) and the different geographic settings could explain the difference. No specific literature regarding modelling targeted high-risk MSM screening was found.

In our model, high-risk MSM are modeled as a function of each agent's age and sexual activity level; with high-risk MSM being those who are younger and more

sexually active. High-risk MSM are often defined in the literature by their age and risk behaviors such as unprotected anal intercourse and multiple sexual partners.[90] Prior studies on high-risk and young MSM (YMSM) suggest that the level of screening in this population is slightly higher than that of the general population, but not as high as it should be given the increased risk of HIV acquisition.[91] YMSM are more likely to be unaware of their HIV infection, and this in combination with the higher likelihood of having more sexual partners, suggests that YMSM can have a high probability of transmitting HIV to a large number of persons in the MSM community.[91] Young MSM are also more likely to have multiple casual sexual partnerships[92,93], and have unprotected sex[93], and meet partners over the internet.[93] All of these factors in conjunction form a risk environment that favors the increased transmission of HIV and other STIs relative the general population and general MSM population.[90] Therefore, not surprisingly given the increased risk and transmission in this population , increasing HIV testing and NG/CT testing and treatment in this population can greatly decrease the incidence of these two diseases.

In tandem, the results illustrate that targeted screening to high-risk MSM has the most impact amongst these three scenarios. Given that majority of high-risk MSM in model are younger men, and the high HIV prevalence and risk of acquisition has been documented 92, targeted them is not entirely unsurprising. As such, the model results suggest it may be more efficient and impactful to target high-risk MSM for increased HIV and NG/CT screening, rather than pursuing a general HIV testing campaign in the MSM community. Not only are greater reductions in HIV and NG/CT incidence seen, but these results are achieved by giving thousands less HIV and NG/CT tests. Since this

result is achieved by giving less tests, this in turn could potentially lessen person-hours and cost to HIV and NG/CT control programs. Thus, the combination of improved outcomes in decreased incidence and achieving this by screening less MSM, suggest that targeting high-risk MSM is the more efficacious screening strategy.

While the model did approximate the impact of increased screening strategies, the actual process of increasing persons screened was not studied. Thus, while the model shows the benefits of increasing screening, the potential changes to achieve this could be difficult to put into practice. There is a plethora of literature on barriers to improving HIV and STI screening, ranging from racial and stigma related barriers, to cost and ease-of-access barriers.[94] Further complicating matters is that model's suggestion that targeting high-risk MSM for increased screening is most effectives involves a difficult and hard to reach population of the MSM community. Not only could achieving increased targeted screening be difficult, but also potentially more expensive, as the cost to reach and test this population is greater than the cost of pursuing a general HIV testing strategy in the MSM community. However, the model suggests that less MSM need to be screened to achieve greater reductions in incidence, and thus money saved by testing less persons could mitigate the potential increased cost of seeking out this population. This cost-benefit and feasibility analysis should be done to determine the efficacy of pursuing this targeted strategy in practice.

As with all modeling studies, one key limitation is the model necessarily oversimplifies very complex disease dynamics While our model is parameterized to Baltimore City data, it is unlikely that the true magnitude of what transpired in the model will play out exactly in a real-world setting. As such the true impact of these screening

scenarios may be either greater or lesser than the impact seen in the model. While there may be substantial uncertainty regarding the absolute levels of the results here, there may be less uncertainty regarding relative measures (such as the relative impact of screening targeted at high-risk populations versus the entire MSM community more generally). Confounding by race was not accounted or evaluated for in this study. Baltimore is a diverse city, and there are large populations of black and Caucasian MSM. There could be different rates and impacts of each of the screening strategies if we stratify by race due to differing likelihoods of accessing care by race. However, the model does attempt to account for this with a parameter for this racial disparity in HIV care access; and thus the impact of racial differences in HIV care access and screening should be accounted for and have minimal bias.

In conclusion, the study suggests that the most effective screening scenario is one that targets high-risk MSM. The simulation suggests that, depending on extent of screening probability increase, could decrease the incidence of HIV alone by 5-14%, and NG/CT by 5-35%. While the true effect is likely different in the real world, and could face other potential pitfalls given that it targets a hard to reach population, the impact as demonstrated by the model is clear; targeting high-risk MSM for HIV and NG/CT screening can achieve significantly reductions in incidence of these diseases while simultaneously giving less tests. As such, increased attention should be paid towards High-Risk MSM populations going forward in order to produce a larger impact on the HIV and NG/CT epidemics. Thus, this targeted screening strategy, in tandem with other HIV and STI control methods, could help control and eventually help end the HIV and NG/CT epidemic in Baltimore

Tables and Figures

Table 1: List of Parameters

Fixed Parameters	Value	Reference
Partnerships		
Age Mixing: Absolute difference in square root of ages (ADSR) - Stable partnerships - Casual partnerships	 0.6 0.73	[1]
Race mixing: Likelihood of mixing with a partner of the same race - Black-Black - White-White	 0.9 0.75	[1]
Likelihood of condom use - Stable partnerships - Casual partnerships	[Never, Partially, Always] [0.45, 0.55, 0.00] [0.47, 0.12, 0.41]	[1]
Sexual position preference: - Insertive only - Receptive only - Versatile	 0.42 0.26 0.32	[1]
GC		
Proportion of cases symptomatic - Urethral - Rectal - Pharyngeal	 74% 20% 10%	 [2] [3,4] [4,5]
Duration of infection in the absence of treatment	Uniform (3-12) months	[6–20]
Duration of treatment	2 weeks	[6,21,22]
Regular GC screening intervals for HIV+ MSM: - All MSM on ART: - MSM with a recent history of GC in the last 6 months	 12 months 6 months	[23]
Likelihood of compliance with guideline (presenting for scheduled appointment)	35%	[24–29]
Efficacy of condoms to prevent GC transmission	70%	[6,30,31]
Increase in HIV transmissibility (from urethral or rectal infection)	Uniform [1.5-2] fold	[32–36]
Increase in HIV susceptibility (from urethral or rectal infection)	Uniform [1-2.5] fold	[5,6,36,37]
HIV		
Disease state duration		
Acute infection (CD4 >500 cells/μL)	[6, 9] weeks	[38–40]
Chronic infection (CD4 200-499 cells/μL)	[8, 10] years	[38,41]

Late infection (CD4 <200 cells/μL) [1]	[1, 3] years	38,39,41
Time from ART initiation to full viral suppression	[4-24] weeks	42
Maximum duration of time to stay in late state after ART initiation before reverting to chronic state	52 weeks	
Time from ART discontinuation to pre-ART CD4 nadir[2]	ART treatment duration up to one year[b]	43–46
Mortality rate [3] Acute and chronic, no ART Late, no ART Reduction in mortality due to ART[3]	 5 per 1000 person years 1/duration of late infection 0.58% per week	47–49
Average viral load (log10 copies/mL) Acute, no ART Chronic, no ART Late, no ART On ART, partially suppressed On ART, fully suppressed	 6.5 4.5 5 3.5 1.5	38
Efficacy of condoms to prevent HIV transmission	80%	50,51
Infectiousness for HIV per sexual contact	2.45 (log(VL)-4.5)	38
Annual probability of engagement in HIV care	.3[c]	52–54
Weekly probability of ART discontinuation	0.015[d]	55
Minimum gap in care after ART discontinuation	26 weeks	56
Parameters calibrated to population-level surveillance data		
Site specific probability of NG/CT transmission per act - Urethral - Rectal - Pharyngeal	 0.35 0.49 0.16	
Weekly probability of symptomatic NG/CT testing - Urethral - Rectal - Pharyngeal	 0.009 0.001 0.04	
Background rate of screening MSM for HIV and NG/CT	0.014	
Proportion of MSM screened for NG/CT annually	.40	
Probability that NG/CT screening occurs only at urethral site	0.93	
Weekly probability of: - Screening for HIV only - Linkage to care (if HIV-positive and not linked)	 0.0024 0.007 0.08	

A: Mortality rate in late infection is defined as 1/(duration in the late infection disease state.

B Infectiousness assumed equal to that of the chronic state

D If a person start ART during the chronic state, they'll mortality level will be immediately reduced according to this cofactor. However, if he start ART in the later state, he'll be subjected to the late state mortality level for a period of time before reverting back to the chronic state. This duration is estimate as the time spent in the late state up to one year. once in the chronic state, the person will be subjected to the baseline mortality level of 5 per 1000 p/y times the ART cofactor.

- Starting ART (if linked to care) - Disengagement from care (if linked to care)	0.002
Relative likelihood of accessing HIV care among Black MSM	0.5

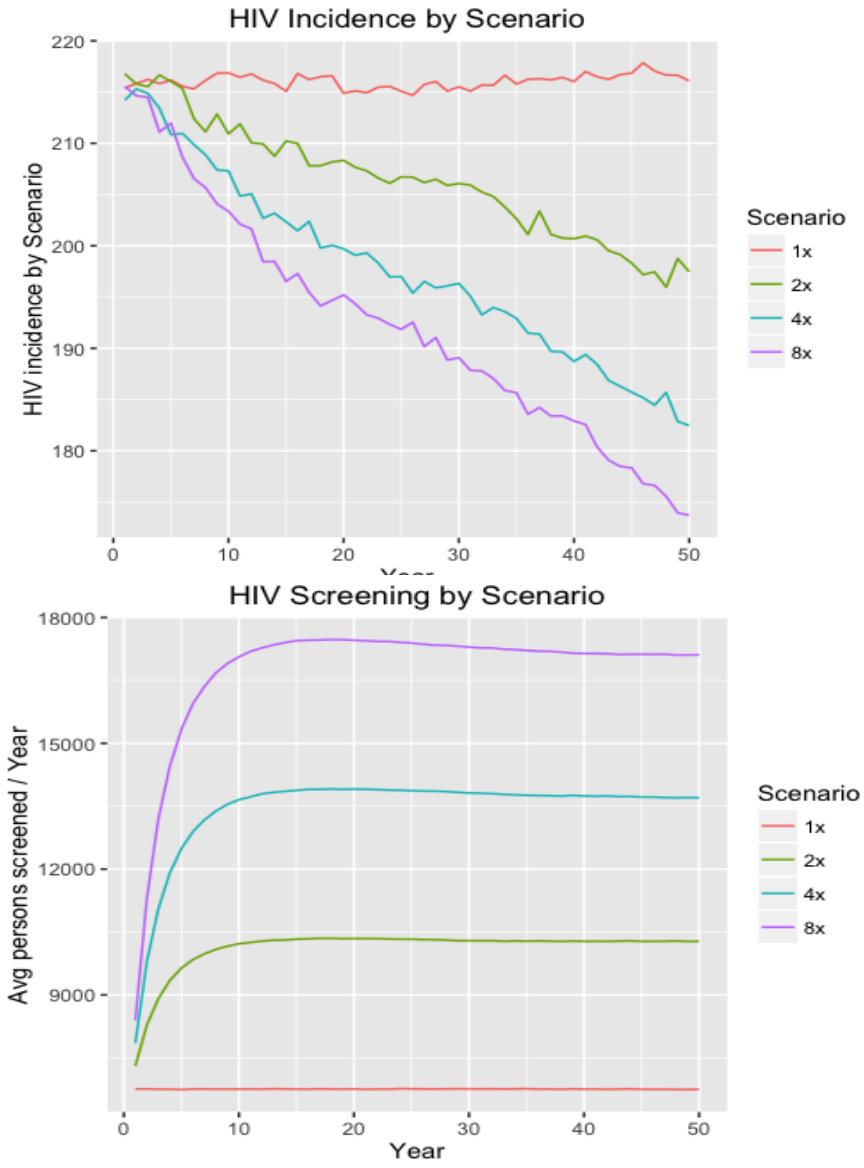
Table 2: Contrasting Screening Strategies Results on HIV Rates

	Targeted Screening for High-risk MSM			General HIV Screening		
	2x	4x	8x	2x	4x	8x
Avg. number of HIV tests given per year	10,116	13,437	16,733	9,368	14,596	25,051
Incidence Rate per 100,000 persons at year 30	1373	1307/	1260/	1420	1387	1360
IR Percent Decreases Relative to Baseline	4.65%	9.23%	12.50%	0.90%	3.20%	5.10%

Table 3: Contrasting Screening Strategies Results on NG/CT Rates

	Targeted Screening for High-risk MSM			General HIV Screening		
	2x	4x	8x	2x	4x	8x
Avg. number of NG/CT tests per year	7,253	10,586	14,266	NA	NA	NA
Incidence Rate per 100,000 persons at year 30	15007	13000/	11213	17007	16613	16,400
IR Percent Decreases Relative to Baseline	13.72%	25.00%	35.53%	2.07%	4.24%	5.56%

Figures 1a and 1b: HIV Incidence and HIV Tests Given Annually Over a 50-year period for the High-Risk MSM Screening Strategy



Figs 1a and 1b: 1a presents HIV incidence per 15,000 MSM by scenario under the targeted screening of high-risk MSM strategy. 1b presents the total number of HIV tests given per year over a 50 year period

Figure 2: HIV Prevalence Over a 50-year period for the High-Risk MSM Screening Strategy

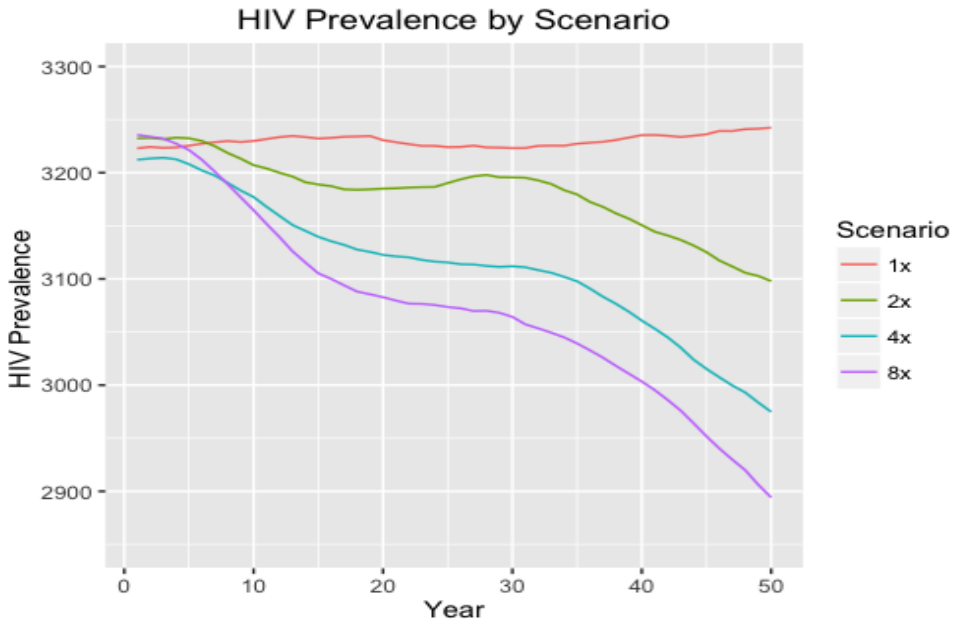


Fig 2: Presents HIV prevalence per 15,000 persons by scenario for each year under the targeted screening of high-risk MSM strategy.

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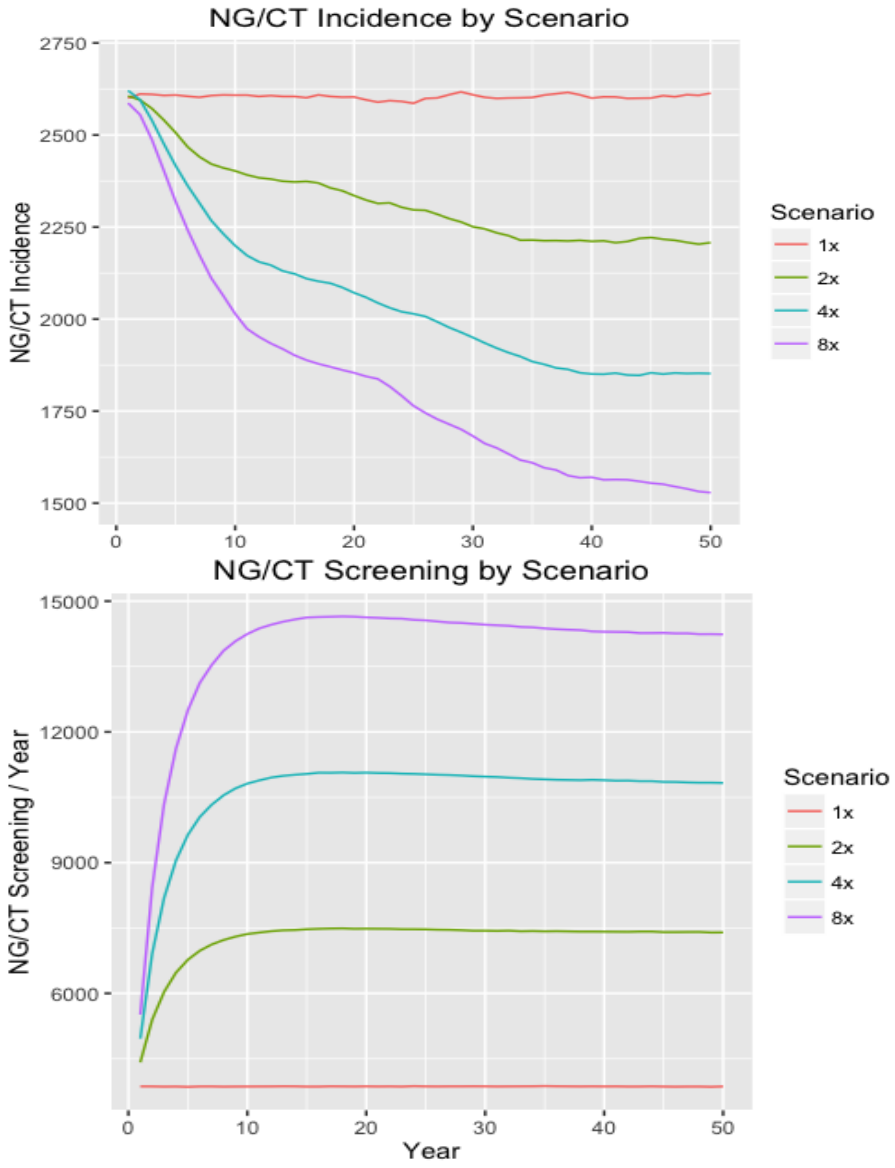
Figure 3: NG/CT Incidence and NG/CT Tests Given Annually Over a 50-year period for the High-Risk MSM Screening Strategy



Figs 3a and 3b: 3a presents NG/CT incidence per 15,000 MSM by scenario under the targeted screening of high-risk MSM strategy. 3b presents the total number of NG/CT tests given each year by scenario under the same strategy.

Figure 4: NG/CT Prevalence Over a 50-year period for the High-Risk MSM Screening Strategy

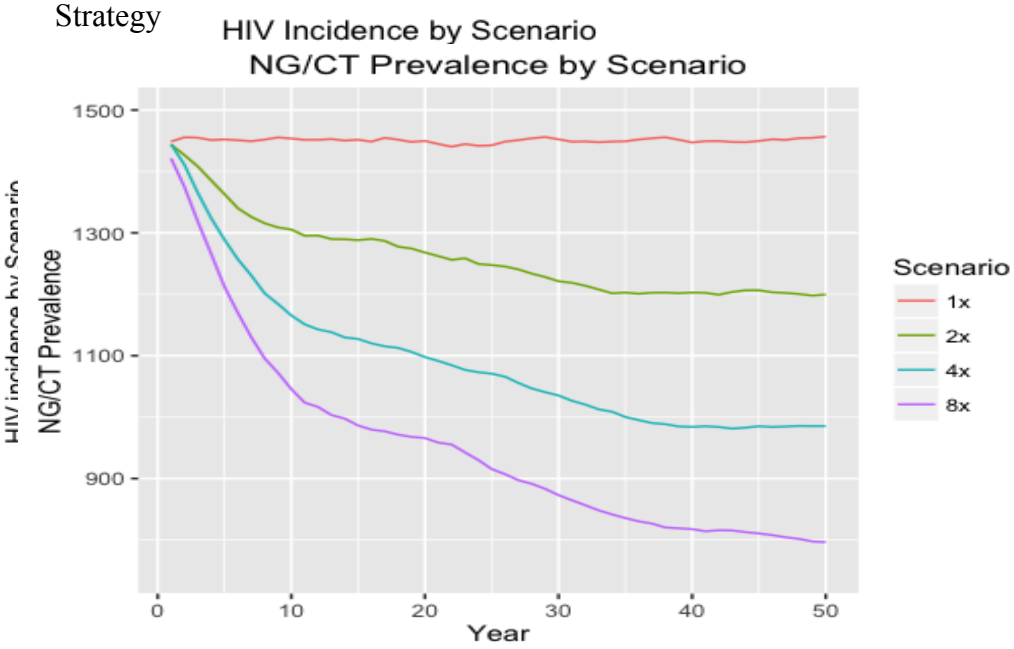
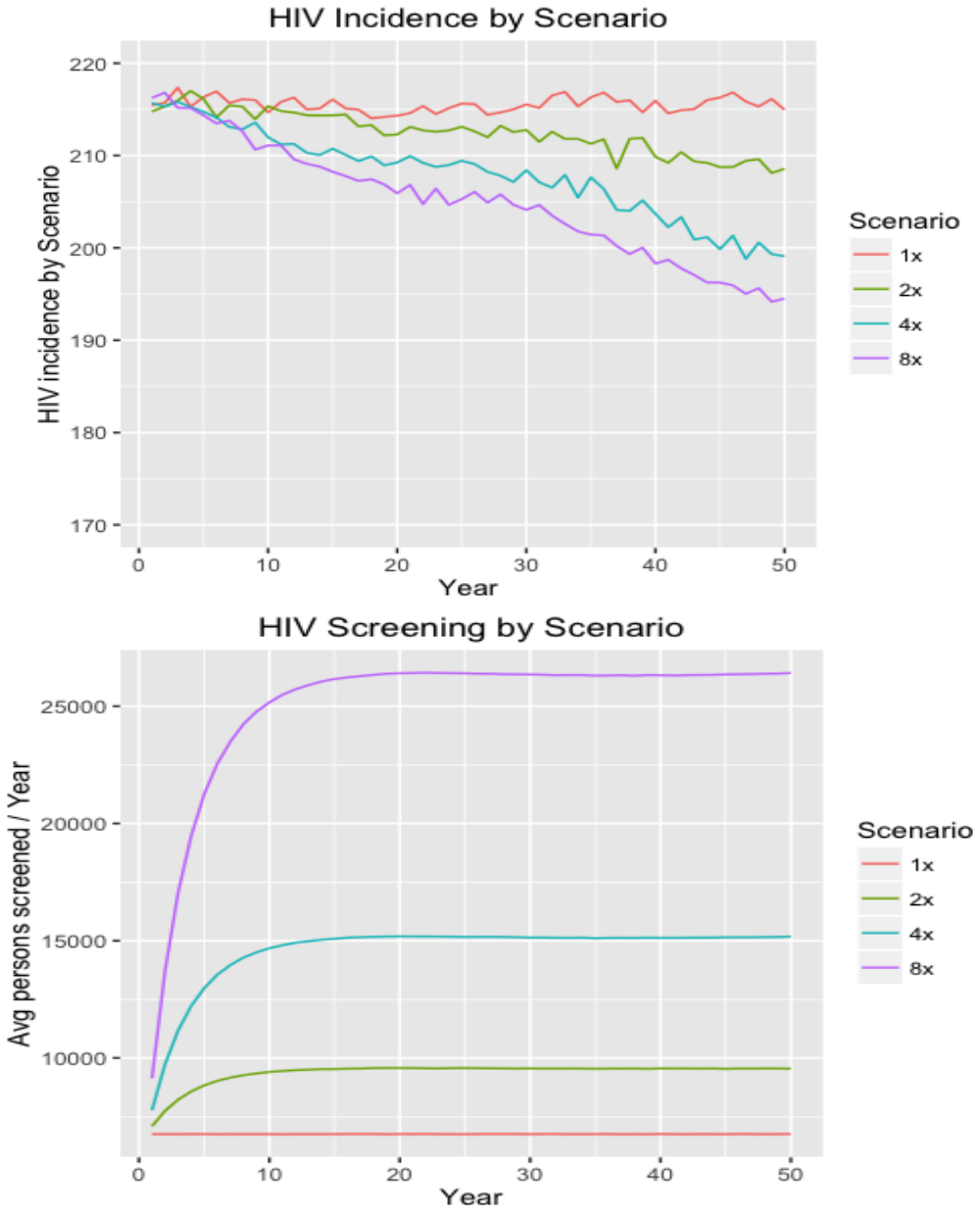


Fig 4: Presents NG/CT prevalence per 15,000 persons by scenario for each year under the targeted screening of high-risk MSM strategy.

Figures 5a and 5b: HIV Incidence and HIV Tests Given Annually Over a 50-year period for the General HIV Screening Strategy



Figs 5a and 5b: 5a presents HIV incidence per 15,000 MSM, by scenario under the increased general HIV screening strategy. 5b presents the total number of HIV tests given each year by scenario under the same strategy.

Figure 6: HIV Prevalence Given Annually Over a 50-year period for the General HIV Screening Strategy

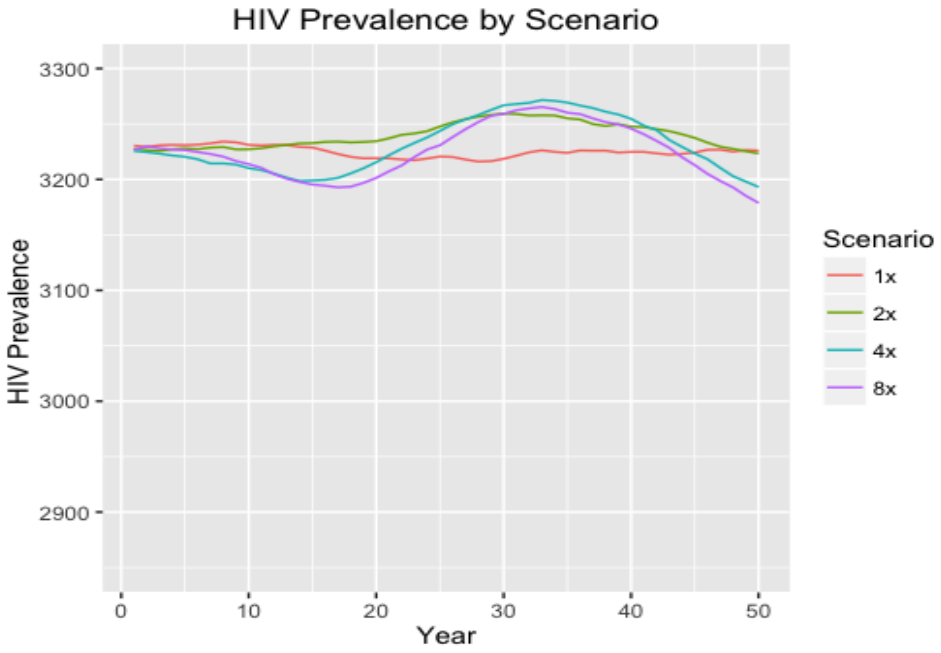


Fig 6: HIV prevalence per 15,000 persons by scenario for each year under the increased general HIV screening strategy.

Figure 7: NG/CT Incidence Over a 50-year period for General HIV Screening Strategy

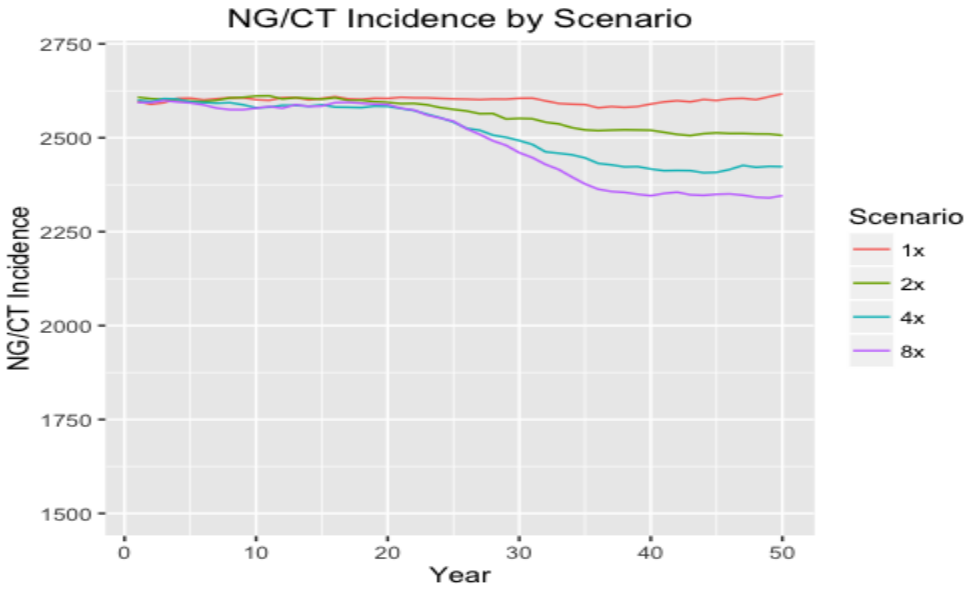


Fig. 7 presents NG/CT incidence per 15,000 MSM for each year by scenario under the increased general HIV screening strategy

Figure 8: NG/CT Prevalence Over a 50-year period for the General HIV Screening Strategy

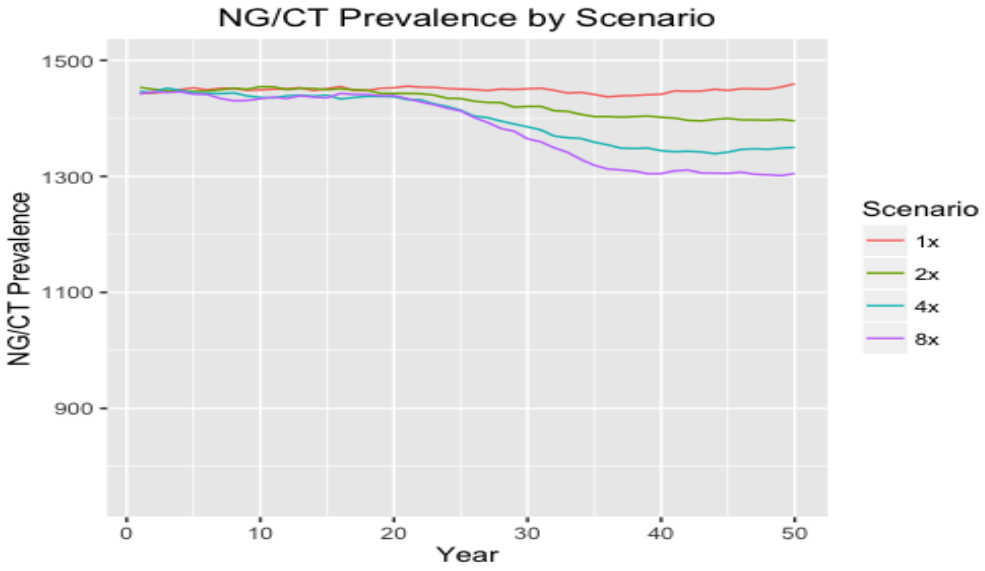


Fig 8: Presents NG/CT prevalence per 15,000 persons by scenario for each year under the increased general HIV screening strategy.

Figure 9: HIV Incidence Over a 50-year period for the Increasing NG/CT Screening Amongst HIV Infected MSM Strategy

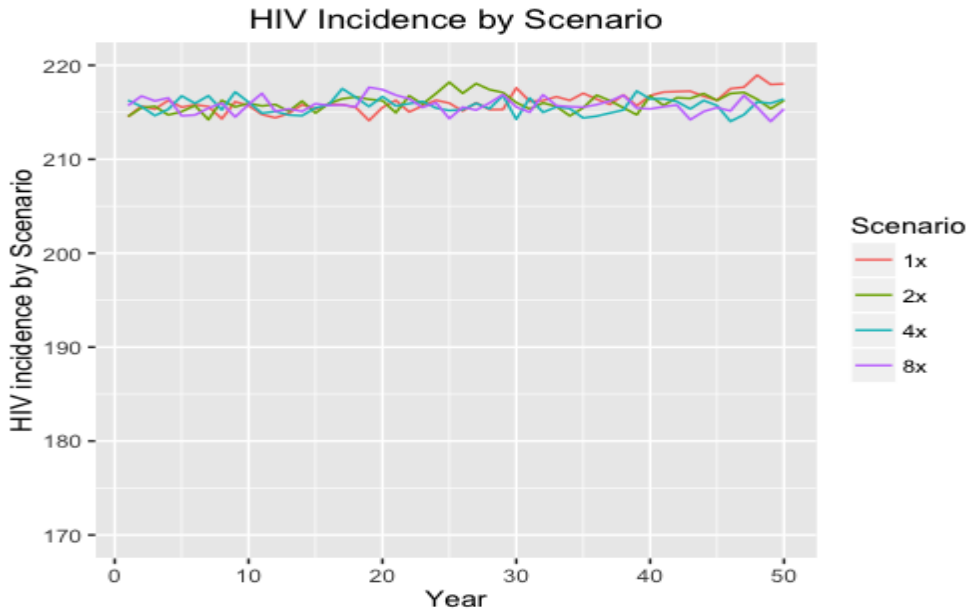


Fig 9 presents HIV incidence under the increased NG/CT screening strategy for 15,000 MSM for each year by each scenario.

Figure 10: HIV Incidence Over a 50-year period for the Increasing NG/CT Screening Amongst HIV Infected MSM Strategy

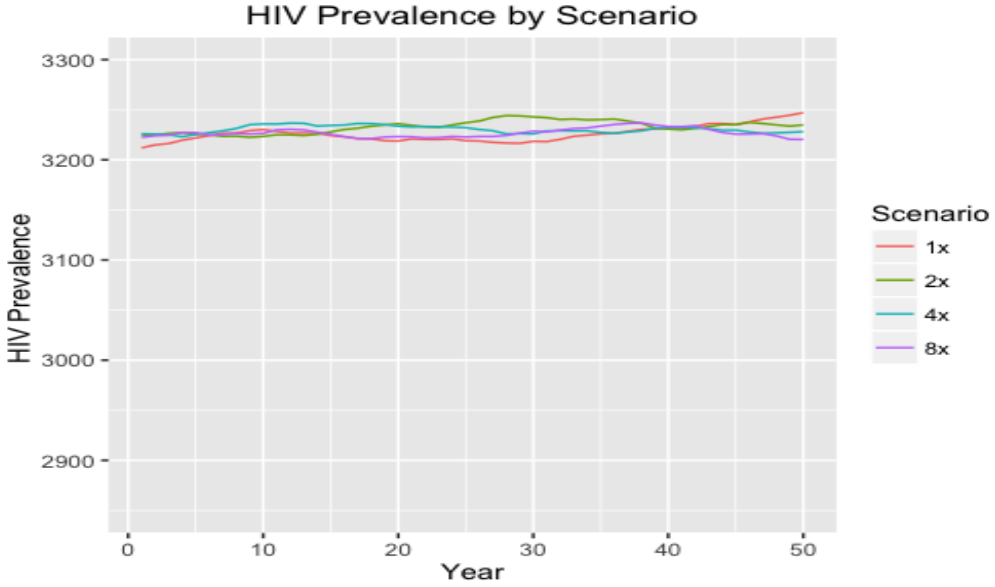
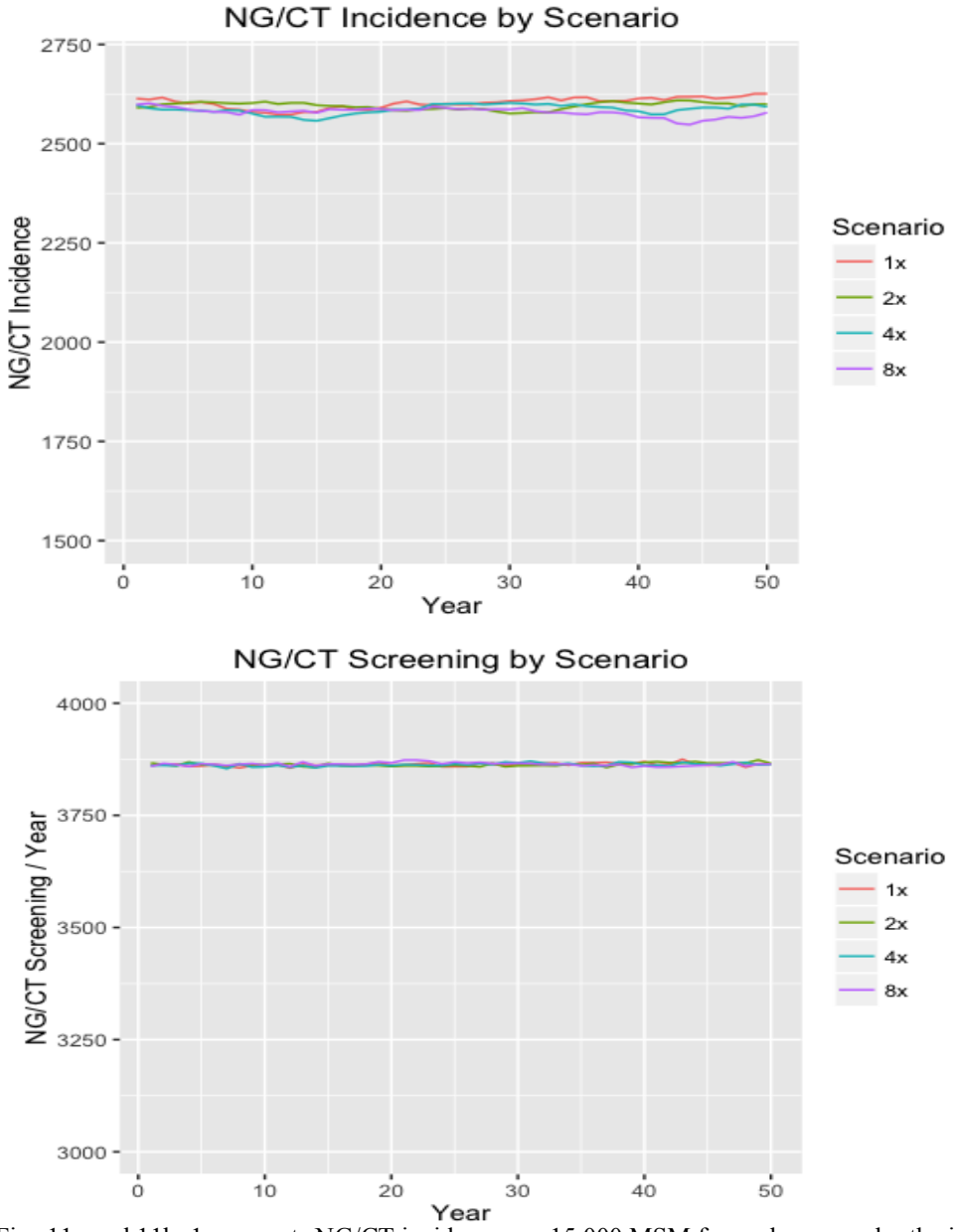


Fig 10: Presents HIV prevalence under the increased NG/CT screening strategy per 15,000 persons by scenario for each year.

Figures 11a and 11B:NG/CT Incidence and Number of MG/CT Tests Given Annually Over a 50-year period for the Increasing NG/CT Screening Amongst HIV Infected MSM Strategy



Figs 11a and 11b: 1a presents NG/CT incidence per 15,000 MSM for each year under the increased NG/CT screening strategy.1b presents the total number of MSM screened each year for NG/CT under the same strategy

Figure 12: NG/CT Prevalence Over a 50-year period for the Increasing NG/CT Screening Amongst HIV Infected MSM Strategy

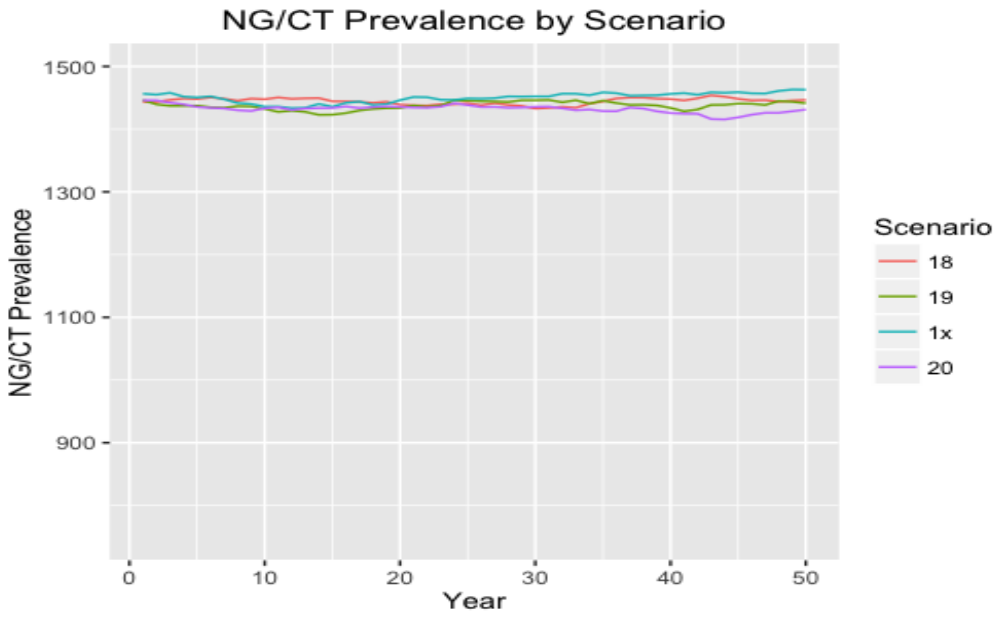


Fig 12: Presents NG/CT prevalence per 15,000 persons by scenario for each year under the increased NG/CT screening strategy

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EDUCATION

Harvard University, T.H. Chan School of Public Health — Boston, MA
Department of Immunology and Infectious Diseases
Doctor of Philosophy (Ph.D.) in Biological Sciences in Public Health — Expected January 2023

Johns Hopkins University, Bloomberg School of Public Health — Baltimore, MD
Department of Epidemiology
Masters of Science (Sc.M.) in Infectious Disease Epidemiology — May 2017

Emory University, College of Arts and Sciences — Atlanta, GA
Bachelors of Science in Biology, Minor in Global Health, Culture and Society — May 2015

PROFESSIONAL EXPERIENCE

Johns Hopkins Bloomberg School of Public Health, Department of Epidemiology — Baltimore, MD
Research Assistant — September 2016 – May 2017

- Conduct research on using agent-based modeling to simulate outbreaks of HIV and Syphilis among MSM to better understand the co-infection epidemiology, and how various interventions will affect outbreak dynamics
- Work under Dr. David Dowdy and Dr. Parastu Kasaie

Ragon Institute of MGH, MIT, and Harvard — Boston, MA
HIV Epidemiology and Biostatistical Modeling Graduate Intern — May 2016 – August 2016

- Learned multivariate analysis, dimension reduction, and other machine learning methods, to analyze epidemiological and immunological data for HIV research in R software
- Learned R programming
- Learned genomic analysis of HIV using MacVector
- Project focused on longitudinal multivariate analysis of immunologic data to learn what immunological factors predicted generation of broadly neutralizing antibodies to HIV. Used nonlinear mixed modeling and LASSO techniques to identify these associated factors.

Johns Hopkins Bloomberg School of Public Health, Department of Epidemiology — Baltimore, MD
Research Assistant — November 2015 – May 2017

- Assistant at the Johns Hopkins Biological Repository
- Training in CD4 cell count measurement, HIV viral load measurement, HCV serological testing, PBMC harvesting, sample management software and phlebotomy.
- Help provide laboratory assistance to various HIV cohort studies run by JHSPH.

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Baltimore, MD
Research Assistant — September 2015 – March 2017

- Assisting on a project to explore the use of dried blood spot (DBS) analysis as a diagnostic tool for toxic industrial chemical (TIC) occupational exposures in the dense, urban operational environment; and to develop an informatics-informed risk assessment environment for DBS inclusion aimed at recognition and control of disaster-related TIC occupational exposures.

- Used systematic review software to assist in literature review of DBS applications

The Council For Responsible Genetics New York, NY
Policy Research Intern May 2014 - August 2014
- Researched and wrote a policy report reviewing high containment laboratory and biosecurity policy in the United States, specifically focusing on the San Francisco Bay Area, the growth the biotechnology industry there, and the risks associated with this expansion.

The Carter Center Atlanta, GA
Research Assistant September 2013- May 2015
- Orchestrated research into the cost effectiveness of integrating disease control programs
- Drafting an original manuscript for publication about integrating Trachoma control and Guinea Worm Disease eradication programs

Emory University, Rollins School of Public Health Atlanta, GA
Lab Research Assistant August 2013 – May 2015
- Conducted research about the epidemiology of meningitis in the Atlanta area
- Using GIS software to map cases of meningitis over a 20 year period in order to analyze patterns in disease transmission
- Built a Poisson model using SatScan to analyze the temporal and spatial trends of meningitis in the Atlanta area to retrospectively identify clusters of disease.

The Carter Center Atlanta GA
International Health Programs Intern June 2013 - August 2013
- Assisted in a literature review for a paper on the control of Onchocerciasis and how it's control helps achieve the Millennium Development Goals

New York University School of Medicine, Department of Rheumatology New York, NY
Intern/ Lab Research Assistant Summer 2009 and 2010
- Conducted experiments into researching biomarkers for fetal heart block in lupus patients and mastered lab techniques including Western blots, tissue cultures, and assays.
- Published paper in Rheumatology, titled "A central role of plasmin in cardiac injury initiated by fetal exposure to maternal anti-Ro autoantibodies

TEACHING EXPERIENCE
Emory University
Introduction to Global Health, Teaching Assistant Spring Semester 2015
- TA for class of 170, duties included grading tests, papers, and homework, and holding office hours and review sessions

Johns Hopkins University, Bloomberg School of Public Health
Pubic Health Impact and Epidemiology of HIV/AIDS, Teaching Assistant Fall 2016, 1st Quarter
- TA for class of 70, duties include grading tests, holding office hours, and assisting and providing feedback for student presentation

ACTIVITIES
American Society of Tropical Medicine and Hygiene, Johns Hopkins BSPH Student Assembly Vice President of Social and Cultural Affairs, Epidemiology Student Organization, Johns Hopkins Public Health Mentors, Johns Hopkins BSPH Committee on Equity, Diversity and Civility member, Pi Kappa Alpha.

SKILLS AND INTERESTS
Skills: Lab techniques. Stata Statistical Software, SAS statistical software, R Statistical software, ArcGIS software. Excel (intermediate prof.) Microsoft Word, literature review
Interests: Evolutionary Medicine, Infectious Diseases, Emerging Diseases, Global Health

SELECTED PUBLICATIONS
1. Dunn, Caitlin, Kelly Callahan, Moses Katabarwa, Frank Richards, Donald Hopkins, P. Craig Withers, **Lucas E. Buyon**, and Deborah Mcfarland. "The Contributions of Onchocerciasis Control and Elimination Programs toward the Achievement of the Millennium Development Goals." *PLoS Negl Trop Dis PLOS Neglected Tropical Diseases* 9.5 (2015)
2. Briassouli, P., M. K. Halushka, J. H. Reed, Y. Molad, K. Fox-Talbot**, L. Buyon**, E. Guzman, A. Ludomirsky, R. M. Clancy, and J. P. Buyon. "A Central Role of Plasmin in Cardiac Injury Initiated by Fetal Exposure to Maternal Anti-Ro Autoantibodies." *Rheumatology* 52.8 (2013): 1448-453.

CONFERNCE PRESENTATIONS
Lucas Buyon, Randall Slaven, Paul M. Emerson, Jonathan King, Oscar Debrah, Ernesto Ruiz-Tiben, Kelly Callahan. Achieving the Endgame: Improving Integrated Case Searches for Guinea Worm Disease and Trachoma to achieve Eradication and Elimination Targets. Poster presentation delivered at the American Society of Hygiene and Tropical Medicine Annual Meeting, Atlanta, GA, November 2016